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Review

Epidemiology of Central Nervous System Tumors in Karlovac Area (Croatia), 1995–2010

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A B S T R A C T

The aim of this study was to provide an overview of the central nervous system (CNS) tumours epidemiology in Karlovac region, over the 1995–2010 period. We analyzed data on 359 patients (194 men and 165 women), diagnosed with CNS tumours according to the World Health Organization's diagnostic criteria, in period 1995–2010. The data were obtained from the Neurology and Neurosurgery Department, including other medical records. The data were analysed with t-test and chi-square test. A total of 359 cases of tumours in CNS were recorded for the period of 1995–2010, with slight predominance of men (194;54.0%) over women (165;46.0%). Under the assumption of gender equality, we did not detect a significant gender difference in tumour diagnosis (p=0.279). Mean age at the diagnosis was 64.1±12.6 years, with significant gender difference: mean age at diagnosis for men was 62.8±11.6 years, while for women it was 65.7±13.5 (p=0.029). The commonest type of all tumours was metastases (144;40.1%). When only primary tumours were analysed, the commonest type was glioblastoma (125;58.15%), followed by meningeoma (44;20.5%). The remaining types were much less frequent, with i.e. 5 recorded cases of the following three types: astrocytoma, ependimoma and oligodendroglyoma (2.3%). These results suggest a commonly encountered epidemiological profile in the region, with commonest metastases, and glioblastoma as the most common primary tumour. Due to difficulties related to patient gravitating hospitals admittance and overall small sample size for more detailed analyses, it remains for future studies to determine potential association of the Homeland war (1991–1995) and the occurrence of CNS tumours.

Key words: *tumour, central nervous system, glioblastoma*

Introduction

Wartime and warfare introduces an entire new set of environmental stresses for the human population experiencing such events. Besides increased physical and psychological risks, the reports of the increased cancer incidence are often heard in the general public. This is especially the case with brain tumours. However, even the long-term evaluations of war veterans from different wars do not provide results that suggest that exposure to conventional warfare may be associated with increased risk of brain tumorous[1–4]. But, exposures to certain specific chemical agents may seem to be associated with increased risk of brain tumorous[1].

Studies of the recent conflict in the Balkans have suggested that incidence of some tumorous may be increased, but this was attributed to population mixing rather than warfare exposure[5]. Certain differences were recorded in the neighbouring Bosnia and Herzegovina region[6–8], but some studies have tried to demonstrate difficulties in estimating epidemiological data from the region during the warfare affected periods[9]. Studies from Croatia have provided a well-established pattern of possible regional differences and established numerous difficulties in exact estimation of incidence rates[10–12]. However, some studies have also established a pattern of extreme increase, despite the fact that the study was undertaken in the region that was not directly affected by the warfare[13,14]. All these facts may further support the notion that such estimates may be extremely difficult to

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establish precisely and that alternative approaches and/or use of the international data may be needed.

The aim of this study was to investigate the pattern of brain tumorous incidence in the Karlovac region of Croatia.

Methods

Data Collection

This study was based on the multiple sources of information, including registers of admissions and discharges of General hospital in Karlovac, Croatia (Department of Neurology), University Hospital Center Zagreb, »Sestre Milosrdnice« University Hospital Center and Dubrava University Hospital (Departments of Neurology, Departments of Neurosurgery, Oncology and Radiotherapy). Additionally, the data was supplemented from databases of the Croatian Institute for Health Insurance[15]. Thee study period encompassed 1995–2010, with all the registered patients included in order to provide a comprehensive account of the epidemiological situation. The study was approved by the local Ethical Committe of the General hospital Karlovac. Demographic data for the Karlovac area were obtained from the Republic of Croatia census for 2001. All adult patients fulfiling the World Health Organization diagnostic criteria for CNS tumorous were included int his study[16].

Statistical Analysis

The data was analyzed as the crude numbers (no rates were caluclated due to difficulties in estimation of total population under the study due to war and extensive migrations). Chi-square test and t-test were used in the data analysis. The data were analyzed using R (http://www.r-project.org), with significance set at $p<0.05$.

Results

A total of 359 cases of tumours in CNS were recorded for the period of 1995–2010, with slight predominance of men (194;54.0%) over women (165;46.0). Under the assumption of gender equality, we did not detect a significant gender difference in tumour diagnosis ($p=0.279$). Mean age at the diagnosis was 64.1±12.6 years, with significant gender difference: mean age at diagnosis for men was 62.8±11.6 years, while for women it was 65.7±13.5 ($p=0.029$). The commonest type of all tumours was metastases (Table 1). When only primary tumours were analysed, the commonest type was glioblastoma (125; 58.15%), followed by meningeoma (44;20.5%). The remaining types were much less frequent, with i.e. 5 recorded cases of the following three types: astrocytoma, ependidimoma and oligodendroglyoma (Table 1).

TABLE 1
BREAKDOWN ACCORDING TO HISTOLOGICAL TUMOROUS TYPE

Tumorous type	N	% (total)	% (only primary)
Metastases	144	40.1%	–
Glioblastoma	125	34.8%	58.1%
Meningeoma	44	12.3%	20.5%
Astrocytoma	5	1.4%	2.3%
Ependimoma	5	1.4%	2.3%
Oligodendroglioma	5	1.4%	2.3%
Angioma cavernosum	3	0.8%	1.4%
Other types	28	7.8%	13.0%
Total	359	–	–

Discussion

The main result of this study suggests that the general pattern of brain tumorous was not substantially different from the remaining parts of Croatia. The results equally pertain to both wartime and post-war period, suggesting that no changes were seen during the war. This result is in line with many pervious findings, while some of the published studies indeed report higher incidence related to wars[8–11]. In one of such reports from Croatia the authors have reported higher incidence in Istria region[10], which was not directly affected by the warfare, but rather served as the region which accepted a number of refugees. One possible explanation of the increased incidence is that the population structure had changed, leading to a falsely positive increase in the tumorous rate. This proposition may seem plausible since exact vital statistics data was unavailable then and all rates were calculated based on the historic population structure, thus possibly leading to the reported incidence rise.

The exact mechanism of the increased brain tumorous incidence during the war is another problematic area. If we assume complex origin of tumorous which requires both susceptibility and environmental unfavourable conditions, we may consider war and warfare as the environmental stressor. But, the very nature of war suggests that there will be different exposures across the population, thus causing possible differences in those who were exposed to various unfavourable conditions. This in turn means that we should probably focus on a more specific population sub-groups, such as those who were also exposed to various other conditions, such as chemical plants and oil refinery burning (which was present in some regions of Croatia) and possibility that others might have been exposed to unconventional warfare agents (claims on use of such agents were often made during the war). All these propositions lead to the conclusion of a highly complex situation, where difficulties in establishing a pattern of changes become obvious. Possible solutions include pooling of the data from different sources and regions, which becomes a problem due to different nature of war and mixture of adjacent exposures. An attempt to provide more reliable source of information related to other exposures may be difficult,

since use of such agents was never formally confirmed. All these limitations may mean that the results presented here may be considered only as a piece of the puzzle and that only when assembled with the similar data from other parts of the country it may be possible to provide a more precise answer.

In conclusion, the results suggest no clear indication of war-related increase in the incidence rates.

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EPIDEMIOLOIJA TUMORA SREDIŠNJEG ŽIVČANOG SUSTAVA U PODRUČJU KARLOVCA (HRVATSKA), 1995–2010

SAŽETAK

Cilj istraživanja je bio utvrditi pojavnost tumora središnjeg živčanog sustava (SŽS) u području Karlovca, u periodu od 1995–2010. Retrospektivno su analizirani podaci 359 pacijenata (194 muškaraca i 165 žena) sa potvrđenom dijagnozom tumora središnjeg živčanog sustava prema dijagnostičkim kriterijima Svjetske zdravstvene organizacije u periodu 1995–2010. Podaci su prikupljeni pretraživanjem elektronskih baza podataka, odjela neurologije i klinike za neurokirurgiju te iz drugih izvora. Podaci su analizirani pomoću t-test i chi-square testa. Ukupno 359 slučajeva tumora središnjeg živčanog sustava je registrirano u periodu od 1995–2010, sa blažom predominacijom muškaraca (194;54,0%) nad ženama (165;46,0). Temeljem pretpostavke o ravnopravnosti spolova, nismo otkrili značajniju razliku u spolu u postavljenim dijagnoizama tumora mozga (p=0,279). Prosječna starost pri postavljanju dijagnoze je bila 64,1±12,6 godina, sa blažom razlikom u spolu: prosječna starost u postavljanu dijagnoze kod muškaraca je bila 62,8±11,6 godina, dok je kod žena bila 65,7±13,5 (p=0,029). Najčešći tip svih tumora su bili metastatski tumori središnjeg živčanog sustava (144;40,1%). Kod analize pojavnosti primarnog tumora mozga, najčešći tip je bio glioblastom (125;58,15%), iza slijedi meningeom (44;20,5%). Ostali tipovi su bili manje učestali, među prvih pet slijede tri tipa: astrocitom, ependimom i oligodendrogliom (2,3%). Ovi rezultati prikazuju epidemiološki profil u regiji gdje su najčešći tumori središnjeg živčanog sustava metastaze, i gliblastom kao najčešći primarni tumor mozga. Zbog poteškoća poput prijema u nadležnu ustanovu te rasapa podataka te malog uzorka, za detaljnije analize ostaje budućim studijama da odrede moguću povezanost Domovinskog rata (1991–1995) i pojavnosti tumora središnjeg živčanog sustava.